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Assessment of factors affecting mortality in patients with percutaneous endoscopic gastrostomy tube placement in the intensive care unit

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ABSTRACT

Aim: It was aimed to evaluate the clinical outcomes, complications, and factors affecting mortality of percutaneous endoscopic gastrostomy (PEG) applied to patients in the intensive care unit (ICU).

Material and Method: PEG procedures which were performed in the ICU between January 2016 and January 2021 and patients' age, gender, comorbidities, trauma history, serum CRP, albumin levels, CRP albumin ratios (CAR), and PEG-related complications were reviewed. Patients were divided into two groups, patients without mortality (Group 1) and patients with mortality (Group 2), and a comparison between groups was made.

Results: Of all patients, 49 (39.2%) patients had mortality. The mean age of the patients in group 2 was 69.57±16.78 years, which was higher than the other group (p<0.001). Nephrological diseases and diabetes were significantly more common in Group 2, whereas neurologic diseases were less common (p=0.005, p=0.005, 0.044, respectively). The median length of stay (LOS) of the patients in Group 1 was 50 days, while the median LOS of the patients in Group 2 was found to be significantly higher, with 81 days (<0.001). The mean CRP of Group 2 was 81.63±54.06, which was higher than the other group, while the mean of albumin was found to be 2.29±0.5 and was lower than Group 1 (p<0.001, p<0.001). The mean CAR of Group 1 was 15.96±16.81, which was significantly lower than that of Group 2 (p<0.001). The optimal CAR cut-off value for mortality discrimination was found to be 20,216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2%, and 76.8% test accuracy. A CAR value of ≥ 20.216 increased the odds of death 9.3-fold (OR 10.385, CI 95% 4.481-24.065, p<0.001).

Conclusion: We suggest that CAR ratio, low albumin, and high CRP levels could be predictors of early mortality. Considering that PEG is an elective procedure, we believe that it can be a safe and effective procedure when nutritional support is provided by alternative means and appropriate conditions are met.

Keywords: Percutaneous endoscopic gastrostomy, complications, CRP/albumin ratio, mortality

INTRODUCTION

The primary indication for enteral and parenteral nutrition is to provide nutritional support to meet metabolic requirements in patients with inadequate oral intake. Enteral feeding is generally the preferred method over parenteral feeding in patients with a functional gastrointestinal (GI) tract due to the associated risks of the intravenous route, higher cost, and the inability of parenteral feeding to provide enteral stimulation and subsequent disruption of the intestinal defense barrier (1,2). It has also been shown that enteric feeding can reduce the risk of bacterial translocation and associated bacteremia. Tube feeding through the gastrointestinal tract is mainly considered in patients with inadequate oral intake who have a functional GI tract and for whom tube placement in the digestive tract can be safely maintained.

Percutaneous endoscopic gastrostomy (PEG) is a common procedure indicated for patients with a normal gastrointestinal function who are expected to require long-term enteral nutrition. However, patients requiring PEG typically have underlying chronic diseases and fragile general health. Although there are currently no established standardized criteria for patients requiring PEG, guidelines published by the American Gastroenterological

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Association recommend that PEG be performed only in patients expected to survive more than 30 days after the procedure (3). Despite ongoing efforts to investigate risk factors associated with PEG-related complications and mortality, there have been many studies that have reported different risk factors (4-7). Furthermore, it should be noted that although the PEG has been shown to be a safer option than radiologic or surgical placement, acute and chronic complications have been reported as well. The 30-day mortality rate after PEG has been reported to be 3.3-23.9% (8). The complication rate with PEG has been reported to be 13.2-42.9% (9,10). Complications, including bleeding, wound infection, tube occlusion, tube leakage, aspiration pneumonia, perforation, and buried bumper syndrome, are associated with PEG (11).

Both high CRP and low albumin levels have been shown to be associated with significantly higher mortality in patients undergoing PEG. High CRP and low albumin levels undoubtedly pose a mortality risk for all surgical procedures (7,12,13)

High serum CRP levels have been associated with inflammatory conditions (14). According to studies, both low albumin levels and high CRP levels are associated with malnutrition (7,15). Furthermore, PEG is performed because low albumin levels are an indicator of malnutrition. However, patients who die within 30 days do not benefit from PEG. Therefore, underlying acute conditions should be identified and mitigated, based on albumin and CRP results.

The combination of albumin and CRP in a single index has previously been suggested, and subsequent studies have demonstrated that the CRP/albumin ratio is more indicative of prognosis than either CRP or albumin alone (16). There has been extensive research on the CRP/albumin ratio as an independent prognostic marker in patients with infections, malignancies, and other diseases (16,17). Kim et al. (17) showed that the CRP/albumin ratio at admission was positively correlated with prognosis in patients with severe sepsis or septic shock treated with early targeted therapy. In a study of elderly patients admitted to the emergency department, a high sensitivity-CRP/albumin ratio at admission to the emergency department was associated with all-cause in-hospital mortality in patients older than 65 years (18). CAR has been shown to be a predictor of mortality in patients with acute pancreatitis (19). Furthermore, CAR has predicted overall survival in various malignancies (20-24). However, there are relatively few studies focusing on critical care patients in the ICU (16). There is only one study in the literature about CAR in patients who underwent a PEG in the ICU, and in this study, it was revealed that CRP/albumin ratio could be used to predict complications and early mortality after PEG placement (25).

The aim of this study was to evaluate the clinical outcomes, complications, and factors affecting mortality of PEG performed in critically ill patients in the ICU of the 3rd level Anesthesia and Reanimation Unit, although it is safe and minimally invasive.

MATERIAL AND METHOD

This study was approved by the Hitit University Non-Interventional Researches Ethics Committee (Date: 02.07.2021, Decision No: 2021-73). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Only the PEG procedures performed by the General Surgery Clinic in the 3rd Stage Anesthesia and Reanimation Intensive Care Unit at Hitit University Medical Faculty Erol Olçok Training and Research Hospital between January 2016 and January 2021 and related patients were reviewed. Of these patients, 125 patients were included in the study excluding patients under the age of 18 years, patients with known hematologic diseases, patients without progression records according to hospital records, and patients with a history of upper gastrointestinal obstructive malignancy. 125 patients' age, gender, known neurological, respiratory, gastrointestinal, nephrological, urological, cardiovascular system diseases, trauma history, length of hospitalization, pre-PEG placement serum CRP and albumin levels, CRP albumin ratio (CAR), intubation status of the patient, tracheostomy status and complications due to the PEG were obtained by retrospectively scanning from the archive system. When evaluating the mortality, the follow-up periods of the patients until discharge from the ICU were taken, and patients who developed mortality during the follow-up period (group 1) and patients who did not develop mortality (group 2) were divided into 2 groups, and these groups were compared.

It was designed as a retrospective study. All statistical analyses were conducted using IBM SPSS Statistics for Windows software (version 26; IBM Corp., Armonk, N.Y., USA). Descriptive statistics were expressed as numbers and percentages for categorical variables, and mean ± standard deviation and median in parentheses for numerical variables. The normal distribution of the data was analyzed via the Shapiro-Wilks test. The relationships between variables were investigated using Pearson or Spearman correlation coefficients depending on the distribution normality of the data. Comparison of numerical measurements according to the study groups for two independent groups was evaluated by Mann Whitney U test for age, LOS, pre-PEG placement serum CRP and albumin levels depending on the data distribution. Ratio comparisons of categorical

variables such as gender, known neurological, respiratory, gastrointestinal, nephrological, urological, cardiovascular system diseases, presence of trauma history, rate of need for change after PEG placement, presence of PEG-related infection, intubation status of the patient, and tracheostomy rates according to research groups were analyzed using chi-square test. ROC curve was used to show the discriminating power of CAR, which was significant in terms of mortality, and cut-off values for markers were found using the area under the curve and Youden's index. The sensitivity, specificity, PPV, NPV, and accuracy values were calculated for these cut-off values. Odds ratio values were calculated according to these cut-offs. The level of statistical significance was considered as p<0.05.

RESULTS

The mean age of 109 patients in the whole group was 62.54±17.93 (65) years. 76 (60.8%) patients were male and 49 (39.2%) were female. Patients' comorbidities, LOS, CRP, albumin, and CAR ratios are shown in **Table 1**.

Complications that developed during and after PEG in patients are shown in **Table 2** and indications for the procedure are shown in **Table 3**. Of all patients, 48 (38.4%) patients underwent tracheostomy during the procedure and 28 (22.4%) patients were intubated during the procedure. Mortality developed in 49 (39.2%) patients. No PEG-related mortality was observed.

Comparison of Patients with and without Mortality

Patients were divided into 2 groups without mortality (group 1) and with mortality (group 2) and comparisons were made between the variables. The mean age of group 1 patients was 58±17.27 (61.5) years and that of group 2 patients was 69.57±16.78 (74) years. Group 2 patients were older with a significant difference (p<0.001). When compared in terms of comorbidities, the incidence of neurological and nephrological diseases was significantly higher in group 1 patients compared to group 2 (p=0.044, p=0.005). The median LOS of group 1 patients was 30 (1-730) days, while it was 81 (4-539) days in the other group. It was longer, with a significant difference (p=<0.001). No significant difference was found between the groups in terms of other comorbidities (**Table 1**).

Table 2: Complications due to PEG

Acute complications	
Bleeding	1 (0.8%)
Ileus	2 (1.6%)
Chronic complications	
Wound infection	2 (1.6%)
Leak-Leakage	4 (3.2%)
Tube blockage	3 (2.4%)
Spontaneous tube removal	2 (1.6%)
Aspiration pneumonia	1 (0.8%)
Buried bumper syndrome	1 (0.8%)

Table 3: Indications for PEG Insertion

Diseases	n=125
Neurological Diseases	63 (50.4%)
Lung Diseases	18 (14.4%)
Malignant Diseases	13 (10.4%)
Nephrological diseases	8 (6.4%)
Cardiovascular Diseases	11 (8.8%)
Trauma	12 (9.6%)

The mean CRP of group 1 patients was 44.67±41.64 (34.84) and that of group 2 was 81.63±54.06 (64.9),

Table 1: Demographic characteristics, comparison between patient groups with and without mortality

Variables	All patients (n=125)	Without mortality (Group 1) (n=76)	With mortality (Group 2) (n=49)	Statistical Significance
Age	62.54±17.93 (65)	58±17.27 (61.5)	69.57±16.78 (74)	<0.001
Gender				0.051
Male	76 (60.8%)	41 (53.95%)	35 (71.43%)	
Female	49 (39.2%)	35 (46.05%)	14 (28.57%)	
Neurological Disease	96 (76.8%)	63 (82.89%)	33 (67.35%)	0.044
Respiratory Disease	18 (14.4%)	8 (10.53%)	10 (20.41%)	0.124
Nephrological Disease	21 (16.8%)	7 (9.21%)	14 (28.57%)	0.005
Malignancy	17 (13.6%)	13 (17.11%)	4 (8.16%)	0.189
Diabetes Mellitus	21 (16.8%)	7 (9.21%)	14 (28.57%)	0.005
Cardiovascular Disease	50 (40%)	26 (34.21%)	24 (48.98%)	0.100
Trauma	12 (9.6%)	8 (10.53%)	4 (8.16%)	0.763
Length of stay (days)	50 (1-730)	30 (1-730)	81 (4-539)	<0.001
CRP	59.16±50.08 (44.2)	44.67±41.64 (34.84)	81.63±54.06 (64.9)	<0.001
Albumin	2.89±1.27 (2.6)	3.28±1.45 (2.95)	2.29±0.5 (2.3)	<0.001
CAR	24.65±23.39 (16.56)	15.96±16.81 (11.02)	38.12±25.82 (30.24)	<0.001
PEG replacement	16 (12.8%)	10 (13.16%)	6 (12.24%)	0.881
PEG-associated infection	2 (1.6%)	0 (0%)	2 (4.08%)	0.152
Number of intubated patients	28 (22.4%)	10 (13.16%)	18 (36.73%)	0.002
Number of patients with tracheostomy	48 (38.4%)	23 (30.26%)	25 (51.02%)	0.020
Mortality	49 (39.2%)			

which was significantly higher (p<0.001). The mean albumin level of group 1 patients was 3.28±1.45 (2.95), while it was 2.29±0.5 (2.3), which was significantly lower than that of the other group patients (p<0.001). The mean CAR was 15.96±16.81 (11.02) in group 1 patients and 38.12±25.82 (30.24) in the other group, with a significant difference (p<0.001) (**Table 1**). No significant difference was found between the two groups in terms of PEG replacement and complications (**Table 1**).

While 10 (13.16%) patients in group 1 were intubated, in the other group, 18 (36.73%) patients were intubated, and a significant difference was found between the two groups, in terms of the intubation rates (p=0.002). 23 (30.26%) patients in group 1 had the tracheostomy, while, in the other group, 25 (51.02%) patients had the tracheostomy, and a significant difference was found between the groups (p=0.02) (**Table 1**).

The efficiency of CAR Value to Predict Mortality

The optimal CAR value to discriminate the groups with and without mortality was analyzed using the area under the ROC curve and Youden's index (AUC 0.792 (0.041), 95% CI 0.710-0.873, p<0.001). The optimal CAR cut-off value for mortality discrimination was found to be 20.216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2%, and test accuracy of 76.8%. A CAR value of ≥ 20.216 was found to increase the odds of death 9.3-fold (OR 10.385, CI 95% 4.481-24.065, p<0.001) (**Table 4**, **Figure 1**).

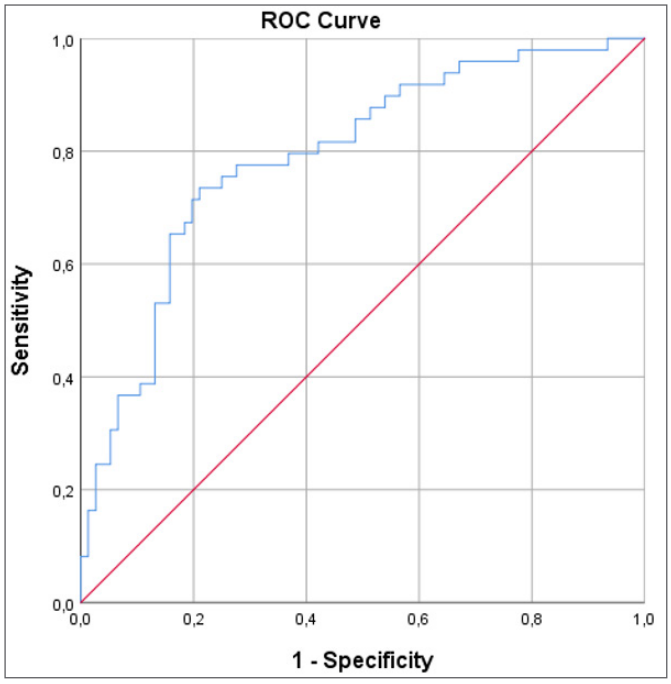

Figure 1: CAR cut-off point and diagnostic values for mortality

DISCUSSION

PEG is usually performed in patients with severe disease, elderly and nearing the end of life. In our study, the median age of the patients who underwent PEG in our study was 65 years. Several studies (4,8,26) have reported comparable results with a median age ranging from 66 to 80 years. The PEG is placed for a variety of conditions that prevent the patient's oral intake or require gastric decompression. It is necessary to define realistic goals and objectives given the indication and the patient's overall medical condition. It is placed to maintain or improve the patient's quality of life (even in the short term), reduce the patient's pain and suffering, and provide access to hydration or medication administration. In the PEG study applied to 80,000 patients, the most common indications for gastrostomy tube placement were a cerebrovascular disease, neoplasms, fluid and electrolyte disturbances, and aspiration pneumonia (27).In this study, neurological diseases (50.4%), pulmonary diseases (14.6%), and malignancy (10.09%) were the most common indications for PEG tube placement. Neurologic dysphagia is one of the most common reasons for PEG tube placement (11, 28).

PEG tube insertion is generally considered a safe procedure, but complications may occur at varying rates depending on the study population. Although procedure-related mortality was low in most studies, the mortality may increase in patients with underlying comorbidities (29). Despite ongoing efforts to assess risk factors associated with PEG-related complications and mortality, several studies have reported different risk factors (4-7). Moreover, although PEG has been shown to be a safer approach than radiologic or surgical placement, the complication rate with PEG has been reported to be 13.2%-42.9% (5,9,10). Complications such as bleeding, wound infection, tube occlusion, tube leakage, aspiration pneumonia, perforation, and buried bumper syndrome (BBS) are associated with PEG (11). In this study, complications developed in 16 (12.8%) patients. This was consistent with the literature.

Bleeding following gastrostomy tube placement is rare. It is usually caused by perforation of the left gastric or gastroepiploic arteries or one of their branches (30). Most bleeding can be controlled by applying simple pressure to the abdominal wound. Endoscopy or surgery should be performed if bleeding persists or if there are significant signs of bleeding such as decreased hemoglobin,

Table 4: CAR cut-off point and diagnostic values for mortality

Variables	Cut-Off	Diagnostic Values					ROC Analysis			Odds Ratio		
		Sensitivity	Specificity	PPV	NPV	Accuracy	Area (SE)	95% CI	p	OR	95% CI	p
CAR	≥20.216	73.5%	78.9%	69.2%	82.2%	76.8%	0.792 (0.041)	0.710-0.873	<0.001	10.385	4.481-24.065	<0.001

aspiration of pure blood from the stomach, melena, hematochezia, or hemodynamic instability. In this study, bleeding occurred in one patient, and gastroscopy was performed due to a decrease in hemoglobin. Besides, it was found that it was not from the stomach and blood products and fluid replacement were performed in the follow-up and it was under control.

Ileus rarely occurs after PEG and the reported incidence is 1%-2% (31). In this study, ileus developed in 2 (1.6%) patients and all patients improved after conservative treatment.

Diabetes mellitus (DM) and old age are considered important risk factors associated with the wound infection after invasive procedures and surgery. Furthermore, DM alters immunity by suppressing polymorphonuclear leukocyte function and cutaneous responses to antigen threats (32).In this study, wound infection developed in 2 (1.6%) patients in the chronic period after PEG. Considering that PEG is an invasive procedure penetrating through the skin into the stomach, wound healing is crucial to prevent infection and tube leakage. In this study, elderly patients with DM who underwent showed significant increases in chronic complications associated with wound healing, with tube leakage being the most common chronic complication in 4 (3.2%) patients.DM and old age may have contributed to tube leakage, which was observed in four patients who presented with signs of inflammation such as redness, pain, swelling, and pus-like discharge at the insertion site. In this study, mortality in patients with DM was significantly higher in Group 2. They found that increased mortality risk after PEG was associated with advanced age, male gender, and diabetes mellitus (8,33).In other studies, various risk factors including high CRP level, low albumin level, advanced age, low BMI, and diabetes mellitus have been reported to be associated with early mortality after PEG (4-8). Our study also supports these studies.

The incidence of feeding tube occlusion has been reported as high as 23%-35%. Risk factors for occlusion include the use of thick enteral feeding formulas, the use of bulking agents, and the use of a smaller diameter feeding tube (8-9 Fr). In this study, occlusion developed in 3 (2.4%) patients. We attribute the lower incidence than the literature to the use of an 18 Fr feeding tube with a larger diameter.

BBS is a serious complication of PEG tube placement that occurs when the internal tampon moves along the stomal tract and outside the stomach wall. This typically occurs as a result of excessive compression between the internal tampon and the external support. The incidence of BBS has been recorded to be approximately 1% (0.3%-2.4%). It occurred in 1 (1.2%) patient in the study and was consistent with the literature.

In this study, no mortality occurred due to the PEG procedure. A mortality rate of 49 (39.2%) was observed in patients with PEG, and it was found that this mortality was associated with high CRP levels, low albumin, elevated CAR, old age, nephrological diseases, diabetes mellitus, intubated patients with and patients with tracheostomy, longer hospitalization, and neurological diseases. Bloomberg et al. (7) found that a CRP level of >10 mg/L and albumin < 3.0 g/dL are independent risk factors for mortality after PEG. Moreover, using these cut-off points, the authors demonstrated 20.5% mortality in patients with high CRP and low albumin levels. In a similar study, the mortality was found to be approximately 60% in patients with a CRP of >21.5 mg/L and albumin of <3.15 g/dL (10). In another study that identified post-PEG CRP elevation as an independent risk factor, an 18% mortality rate was reported at CRP levels >50 mg/L. The cut-off point for low albumin level as an independent risk factor for mortality after PEG in dementia patients has been reported to be 2.8 g/dL (34). In another study, the cut-off points were 78.3 mg/L for CRP and 2.71 g/dL for albumin. Consistent with previous studies, these biomarkers were identified as an independent risk factor for mortality, with 73.1% of patients with high CRP/low albumin levels survived less than 30 days after PEG, which was identified as an independent risk factor for mortality (13). In this study, high CRP and low albumin values were predictive of mortality, which is consistent with the literature.

In this study, the optimal CAR cut-off value for mortality discrimination was 20.216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2% and 76.8% test accuracy (OR 10.385, CI 95% 4.481-24.065, p<0.001). A CAR value of 20.216 and higher increased the odds of mortality by 9.3 times. This is consistent with the literature, and in a study supporting this, it has been suggested that the CRP/albumin ratio can be used to predict complications and early mortality after PEG insertion, and that higher CRP/albumin ratios may help in decision-making in patient selection for the procedure, since PEG is elective (25).

CAR ratio, low albumin and high CRP levels have been previously reported as indicators of malnutrition, inflammation and postoperative infection (7,14,15). Since PEG is not an emergency procedure, it can be postponed; The authors reported that it can be done after investigating an underlying acute condition. In the meantime, nutritional support can be provided with less invasive methods such as parenteral nutrition

or nasogastric catheter (7). PEG should therefore be considered cautiously, particularly in patients with high CRP levels and low albumin levels, as with any elective surgical procedure.

The limitation of this study was that some data were missing from the medical records due to the retrospective design of the study. Besides, the complication and mortality rates were determined by reviewing file alone. Therefore, the possibility of misjudgment of complications and cause of death cannot be ruled out.

CONCLUSION

We suggest that the CAR ratio, low albumin and high CRP levels could be predictors of early mortality. Therefore, underlying acute conditions should be identified and alleviated under the guidance of CAR, albumin and CRP. Considering that PEG is an elective procedure, we believe that it can be a safe and effective procedure when nutritional support is provided by alternative means and appropriate conditions are met.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hitit University Non-interventional Researches Ethics Committee (Date: 02.07.2021, Decision No: 2021-73)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author

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Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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